

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

# PCT

To:

see form PCT/ISA/220

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/EP2004/006888

International filing date (day/month/year)  
23.06.2004

Priority date (day/month/year)  
23.06.2003

International Patent Classification (IPC) or both national classification and IPC  
C12N15/82, C12N15/29, C07K14/415, A01H5/00, A01H5/10

Applicant  
BAYER BIOSCIENCE N.V.

**1. This opinion contains indications relating to the following items:**

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

BEST AVAILABLE COPY

Name and mailing address of the ISA:



European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 epmu d  
Fax: +49 89 2399 - 4465

Authorized Officer

Kania, T

Telephone No. +49 89 2399-7703



**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

10/561793  
IAP9 Rec'd PCT/PTO 21 DEC 2009  
International application No.           
PCT/EP2004/006888

---

**Box No. I Basis of the opinion**

---

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.  
☐ This opinion has been established on the basis of a translation from the original language into the following language \* , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:  
☒ a sequence listing  
☐ table(s) related to the sequence listing
  - b. format of material:  
☒ in written format  
☒ in computer readable form
  - c. time of filing/furnishing:  
☒ contained in the international application as filed.  
☒ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/EP2004/006888

---

**Box No. II Priority**

---

1. ☒ The following document has not been furnished:

- ☒ copy of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(a)).
- ☐ translation of the earlier application whose priority has been claimed (Rule 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

---

**Box No. IV Lack of unity of invention**

---

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has:

- ☐ paid additional fees.
- ☐ paid additional fees under protest.
- ☐ not paid additional fees.

2. ☒ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is

- ☐ complied with
- ☒ not complied with for the following reasons:

**see separate sheet**

4. Consequently, this report has been established in respect of the following parts of the international application:

- ☒ all parts.
- ☐ the parts relating to claims Nos.

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/EP2004/006888

---

**Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

---

1. Statement

Novelty (N)	Yes: Claims	2,3,5,6,8,9,13-17,28,31
	No: Claims	1,4,7,10-12,18-27,29,30
Inventive step (IS)	Yes: Claims	5,6
	No: Claims	2,3,8,9,13-17,28,31
Industrial applicability (IA)	Yes: Claims	1-31
	No: Claims	

2. Citations and explanations

**see separate sheet**

---

**Box No. VIII Certain observations on the international application**

---

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

The present written opinion refers to the following documents cited in the search report:

- D1: DATABASE INTERNET [Online] [www.arabidopsis.org/news/events.jsp](http://www.arabidopsis.org/news/events.jsp); ABSTR. 5-29 2002, VANCANNEYT G. ET AL.: "Podshatter resistance: exploitation of Arabidopsis genes to develop a productivity trait in oilseed rape" retrieved from XIII INTERNATIONAL CONFERENCE ON ARABIDOPSIS RESEARCH, SEVILLA, SPAIN, JUNE 28-JULY 02; 2002
- D2: WO 01/79517 A (UNIV CALIFORNIA) 25 October 2001 (2001-10-25)
- D3: WO 99/00502 A (UNIV CALIFORNIA) 7 January 1999 (1999-01-07)
- D4: WO 01/59122 A (INST OF MOLECULAR AGROBIOLOGY ; SUNDARESAN VENKATESAN (SG); RAJANI SAR) 16 August 2001 (2001-08-16)
- D5: RAJANI SAROJAM ET AL: "The Arabidopsis myc/bHLH gene alcatraz enables cell separation in fruit dehiscence" CURRENT BIOLOGY, vol. 11, no. 24, 11 December 2001 (2001-12-11), pages 1914-1922, ISSN: 0960-9822
- D6: LILJEGREN SARAH J ET AL: "SHATTERPROOF MADS-box genes control seed dispersal in Arabidopsis" NATURE (LONDON), vol. 404, no. 6779, 13 April 2000 (2000-04-13), pages 766-770, ISSN: 0028-0836
- D7: YU HAO ET AL: "AGAMOUS-LIKE 24, a dosage-dependent mediator of the flowering signals." PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, vol. 99, no. 25, 10 December 2002 (2002-12-10), pages 16336-16341, ISSN: 0027-8424

### **Subject-matter of the application**

The application relates to the expression of constructs yielding dsRNA in transgenic Arabidopsis and Brassica plants to reduce seed shattering. The dsRNA molecules are directed against genes which are involved in seed shattering and pod dehiscence, e.g. agamous-like genes AGL1 (= Shatterproof 1), AGL5 (= Shatterproof 2), Indehiscent (IND) and Alcatraz. The technical achievement appears to reside in the use of either weak promoters for the expression constructs or in the employment of dsRNA molecules which have an identity to the target gene of 60-80 %. The effect gained by said methods is that seed shattering is avoided, however, a sufficient threshability remains and pods can be opened by weak physical impact.

### **Item IV: Non unity**

The present set of claims does not fulfill the requirements of unity of invention.

**Article 3(4)iii PCT and Rule 13.2 PCT** stipulate that where a group of inventions

is claimed the requirements of unity shall be fulfilled only where there is a technical relationship among those inventions involving one or more of the same corresponding special technical features. "Special" technical features are those features that define a contribution which each of the inventions makes over the prior art.

The technical feature common to all inventions of the present application is that they relate to plant genes which are involved in the seed shattering process. Any of the documents D2-D6 cited herein discloses said plant genes and uses thereof for the prevention of seed shattering. This feature thus cannot provide a unifying common contribution which the claimed potential inventions make over the prior art.

In fact, two different problems are underlying the different potential inventions of the present application. The first problem is the provision of alternative methods for the prevention of seed shattering in plants by suppression of genes involved therein. The solution being expressed by the first subject of the application.

The second problem may be defined as the provision of alternative gene sequences encoding for proteins involved in seed shattering in plants. The solution being comprised in subject 2 of the application, i.e. relating to SEQ ID NO:2 and 3 as disclosed herein.

Due to the fact that solutions for two different problems are claimed, i.e. two different potential inventions, the present set of claims is considered to lack unity.

#### **Item 5: Novelty and Inventive step**

1. D1 is an abstract from the International Conference on Arabidopsis Research, which took place in Sevilla in 2002. The abstract teaches experiments using Arabidopsis regulatory genes involved in seed shattering for the development of Brassica plants showing podshatter resistance. The use of an dsRNA approach to achieve this goal is not disclosed in said abstract.

The present description, however, refers to said abstract. On page 3, lines 12-17, it is taught that the silencing of the indehiscent gene by dsRNA has been achieved in Arabidopsis which resulted in almost complete podshatter resistance, facts which were allegedly presented during the said Conference.

The methods of present claim 1 and 18 are not distinguished from said teaching since the same dsRNA approach is being used. In claim 18 said approach is directed to Brassica using Arabidopsis sequences, which has already been

addressed in the cited abstract.

Consequently, present claims 1 and 18, as well as dependent claims 4, 7, 14, 19-27, 30 are not regarded as novel since they had been anticipated already by the above oral presentation (**Article 33(2) PCT**).

2. Moreover, the general use of dsRNA to suppress endogenous genes is commonly known in the art, particularly for plants (see e.g. D7). Even if the said claims were rendered novel over the teaching of D1, the methods and products claimed could not be regarded as inventive. Either of D2-D6 disclose or at least suggest the suppression of the endogenous genes involved in the process of seed dehiscence by different approaches, e.g. sense suppression, antisense suppression, mutation, etc. The employment of an alternative method like dsRNA, which moreover is common knowledge in the art, can only be based on an inventive step if a contribution to the art is provided, i.e. a special technical effect.

The technical effect of the present methods could reside in the fact that suppression of the said genes is reduced to the extent that no complete podshatter resistance is achieved and the pods are still threshable by weak physical impact.

Such an effect, however, does not become apparent from the technical features characterizing the said claims. Further, the use of "relatively weak plant expressible promoters" as claimed in claims 2 and 3 cannot be regarded as such an inventive feature since the said promoters were suggested for use already in e.g. D3 (AGL-1 or AGL-5 promoter).

In absence of those technical features providing the said technical effect, the subject-matter of claims 1-4, 7-27, 30, 31 is not regarded as inventive (**Article 33(3) PCT**).

3. The subject-matter of present claim 28 is regarded as novel since the polynucleotide sequences according to SEQ ID NO:2 and 3 have not been disclosed in the prior art.

Claim 29, however, relates to DNA fragments obtainable from a Brassicaceae plant hybridizing to said molecules under stringent conditions.

The DNA sequence encoding for the indehiscent protein of Arabidopsis (D2) shows 85 % identity to either of said sequences. It has to be concluded that said molecule would hybridize to the claimed molecules under stringent conditions.

Thus, claim 29 is not novel (**Article 33(2) PCT**).

4. Further, the identification and cloning of Brassica homologues for the already known indehiscent encoding molecules from the related species Arabidopsis cannot be regarded to comprise an inventive step. It has to be regarded as entirely obvious for the skilled person to set out for the cloning of said molecules, since Brassica is of agronomical importance and said Brassica molecules may be useful for the modification of seed dehiscence in oilseed rape, which appears to be a demand in the art (see D1-D6).  
Consequently, claims 28-30 are not regarded as inventive (**Article 33(3) PCT**).

**Item VIII: Clarity**

The term "relatively weak plant expressible promoters" used in claim 2 is vague and unclear. Since no reference level of activity for such a promoter is given, it does not become apparent what is meant by the feature "relatively weak".